

Overall Survival (OS)

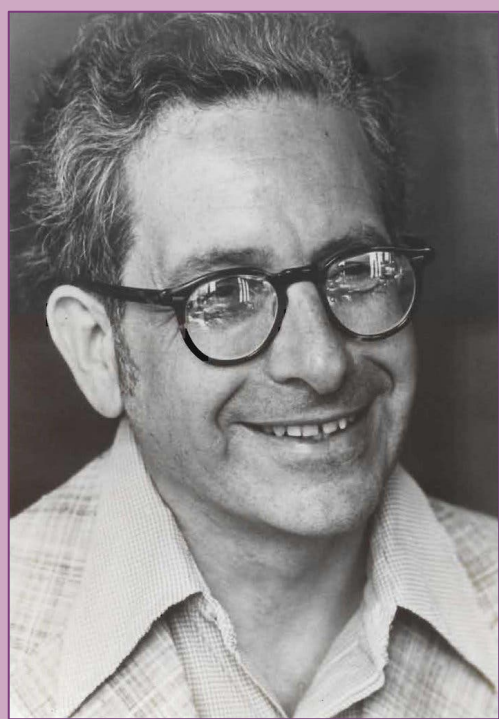
Time from randomization until death from any cause

$AVAL = ADT - STARTDT + 1$   
 $CNSR = \begin{cases} 0, & \text{event} \\ 1, & \text{no event} \end{cases}$

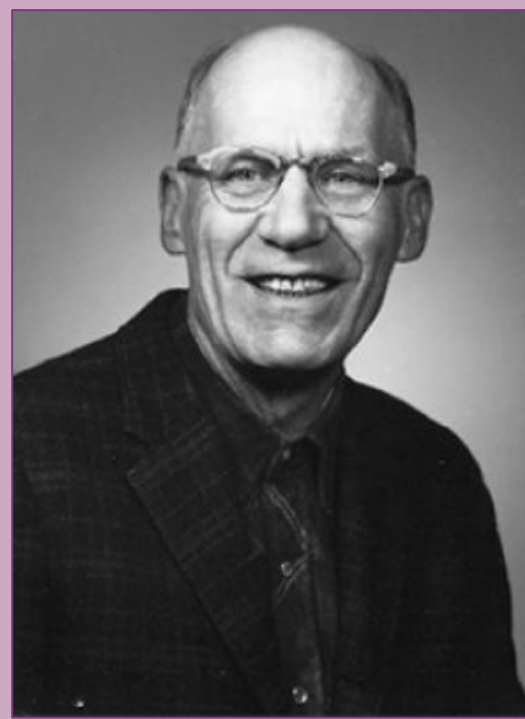
Table 1: Example of CDISC’s ADTTE domain

| USUBJID  | AVAL | STARTDT  | ADT      | CNSR | EVNTDESC           |
|----------|------|----------|----------|------|--------------------|
| 1001-001 | 15   | 01/01/18 | 01/15/18 | 0    | DEATH              |
| 1001-002 | 99   | 01/03/18 | 04/11/18 | 1    | NO EVENT UP TO ATP |
| 1001-003 | 39   | 01/03/18 | 02/10/18 | 0    | DEATH              |
| 1001-004 | 77   | 01/10/18 | 03/27/18 | 0    | DEATH              |
| 1001-005 | 30   | 01/11/18 | 02/09/18 | 0    | DEATH              |
| 1001-006 | 4    | 01/17/18 | 01/20/18 | 0    | DEATH              |
| 1001-007 | 90   | 01/12/18 | 04/11/18 | 1    | NO EVENT UP TO ATP |
| 1001-008 | 28   | 01/01/18 | 01/28/18 | 0    | DEATH              |
| 1001-009 | 31   | 01/09/18 | 02/08/18 | 1    | WITHDRAWAL OF IC   |
| 1001-010 | 91   | 01/03/18 | 04/03/18 | 0    | DEATH              |

In later phase clinical trials, the comparison of **time-to-event** variables is of paramount interest. According to the FDA, **overall survival** (OS) is considered the most reliable cancer endpoint. Everything needed for a **survival analysis**, is stored in **CDISC’s ADTTE** domain. Since an event of interest does not necessarily have to occur in each patient, the observed times might be censored according to prespecified rules. In contrast to other methods, the **Kaplan-Meier estimator** and the resulting **Kaplan-Meier plot** can be used to deal with censored data. Our goal is to show how ADTTE is used as a basis, enabling a valid and well structured evaluation.



Paul Meier  
1924 - 2011



Edward Lynn Kaplan  
1920 - 2006

Kaplan-Meier Approach

The **survival function** describes the population probability of surviving beyond timepoint  $t$ :

$S(t) = P(T > t)$

Table 2: Cumulative structure of the Kaplan-Meier estimator

| Event TP | # at risk | # events | Kaplan-Meier estimate                                                                                         |
|----------|-----------|----------|---------------------------------------------------------------------------------------------------------------|
| $t_1$    | $n_1$     | $d_1$    | $\hat{S}(t_1) = \frac{n_1 - d_1}{n_1}$                                                                        |
| $t_2$    | $n_2$     | $d_2$    | $\hat{S}(t_2) = \frac{n_1 - d_1}{n_1} \times \frac{n_2 - d_2}{n_2}$                                           |
| $t_3$    | $n_3$     | $d_3$    | $\hat{S}(t_3) = \frac{n_1 - d_1}{n_1} \times \frac{n_2 - d_2}{n_2} \times \frac{n_3 - d_3}{n_3}$              |
| $\vdots$ | $\vdots$  | $\vdots$ | $\vdots$                                                                                                      |
| $t_m$    | $n_m$     | $d_m$    | $\hat{S}(t_m) = \frac{n_1 - d_1}{n_1} \times \frac{n_2 - d_2}{n_2} \times \dots \times \frac{n_m - d_m}{n_m}$ |

For  $i = 1, \dots, m$ :  
 $t_i$  : Timepoint of event  
 $n_i$  : Number of subjects at risk at  $t_i$   
 $d_i$  : Number of events at  $t_i$

Table 3: Kaplan-Meier estimates based on sample data

| Event TP | # at risk | # events | Kaplan-Meier estimate                            |
|----------|-----------|----------|--------------------------------------------------|
| 4        | 10        | 1        | $\hat{S}(4) = \frac{10-1}{10} = 0.9$             |
| 15       | 9         | 1        | $\hat{S}(15) = 0.9 \times \frac{9-1}{9} = 0.8$   |
| 28       | 8         | 1        | $\hat{S}(28) = 0.8 \times \frac{8-1}{8} = 0.7$   |
| 30       | 7         | 1        | $\hat{S}(30) = 0.7 \times \frac{7-1}{7} = 0.6$   |
| 39       | 5         | 1        | $\hat{S}(39) = 0.6 \times \frac{5-1}{5} = 0.48$  |
| 77       | 4         | 1        | $\hat{S}(77) = 0.48 \times \frac{4-1}{4} = 0.36$ |
| 91       | 2         | 1        | $\hat{S}(91) = 0.36 \times \frac{2-1}{2} = 0.18$ |

Figure 1: Swimmerplot of the study duration based on sample data

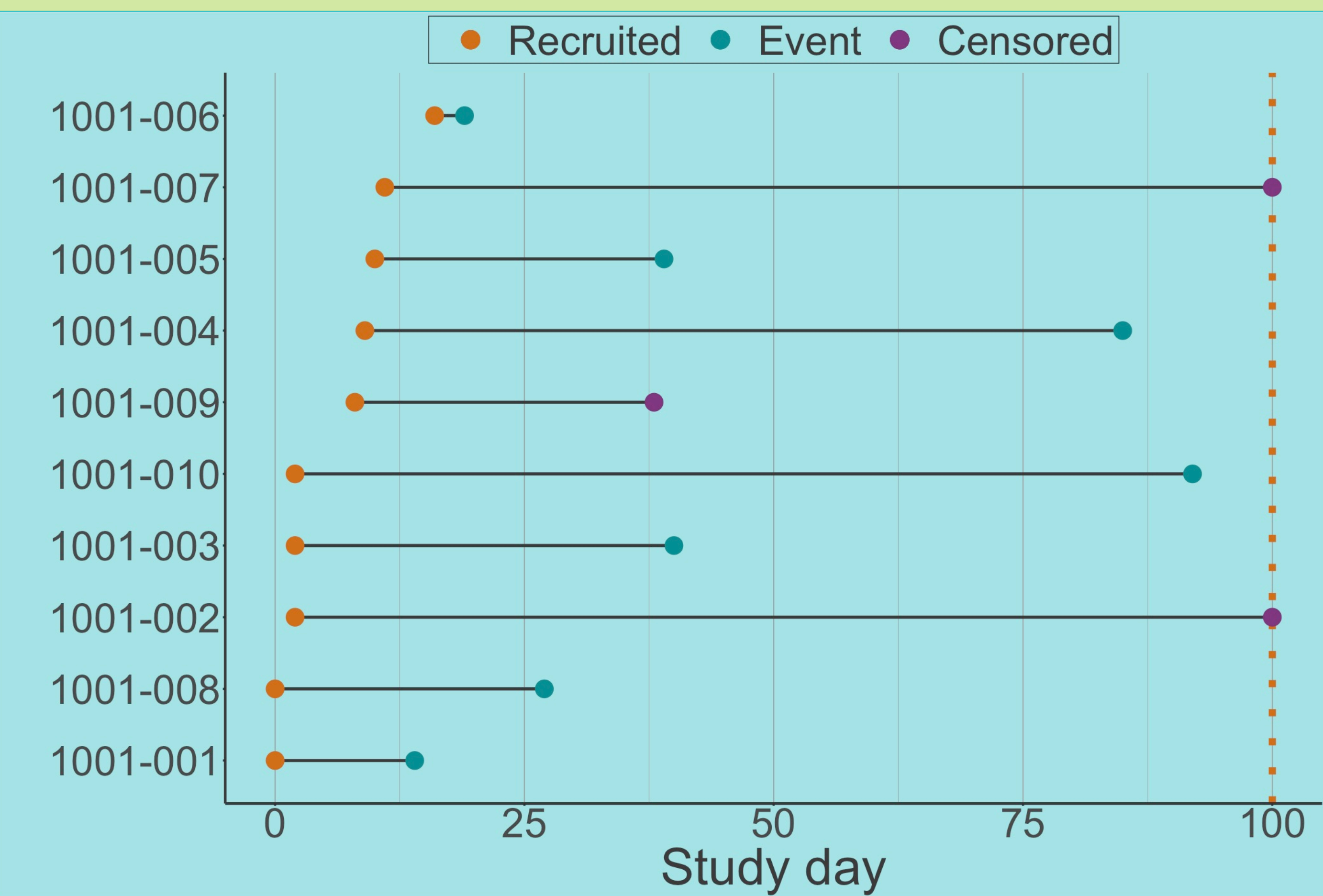
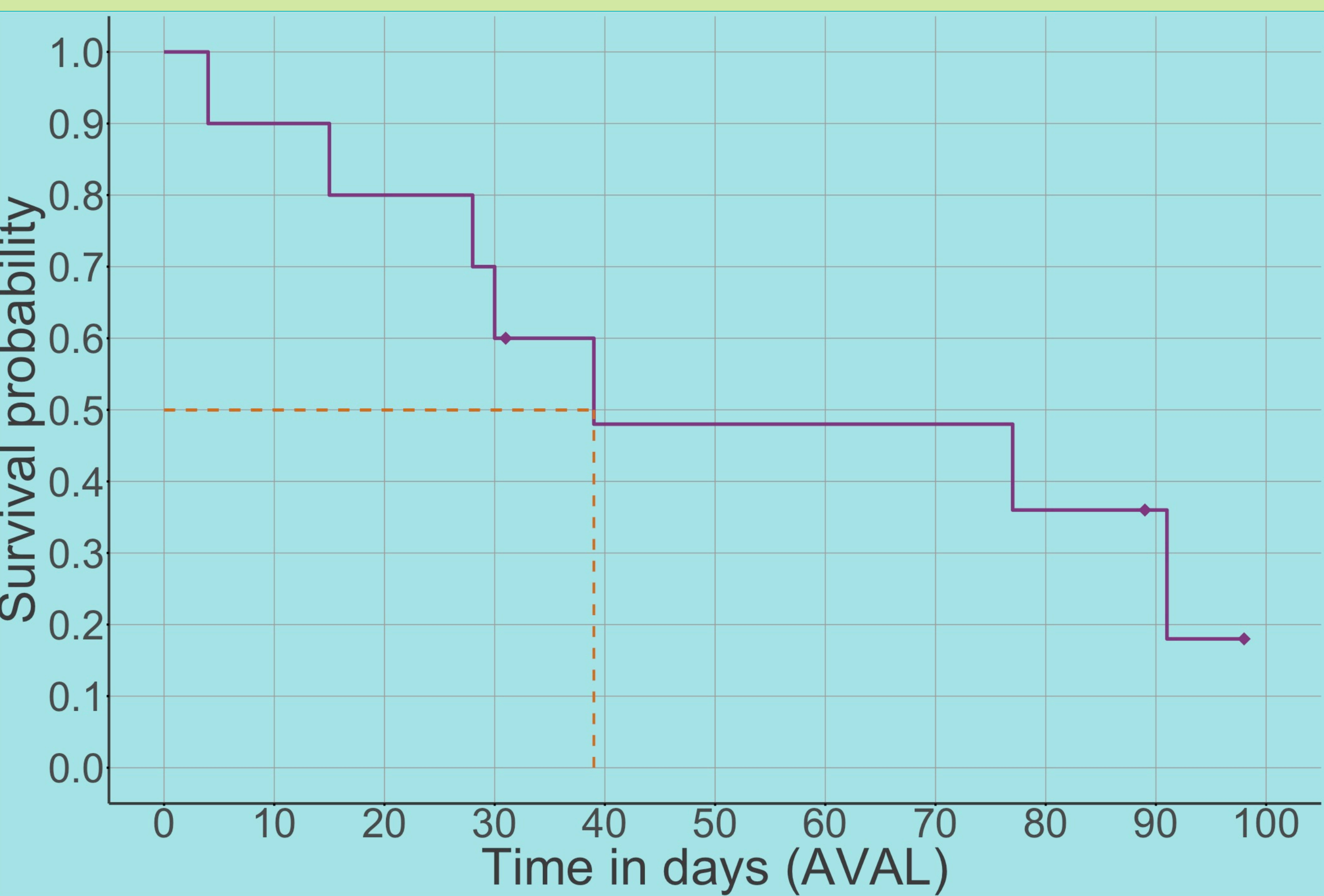


Figure 2: Kaplan-Meier plot of overall survival (OS) based on sample data



Dive in deeper...

- Hazard Ratio
- Progression-Free Survival (PFS)
- Cox Model
- Log-Rank Test
- RECIST
- Proportional Hazards
- Duration of Response (DOR)